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Medical Progress

Adult Respiratory Distress Syndrome

THOMAS L. PETTY, MD, *and* JOHN H. NEWMAN, MD, *Denver*

Adult respiratory distress syndrome is a common respiratory emergency which follows a variety of severe direct and indirect lung insults. Major features are severe respiratory distress, diffuse pulmonary infiltrations, reduced compliance and refractory hypoxemia due to shunt effect. Surfactant abnormalities may play a role in the mechanical derangement of lung function. Supportive care with mechanical ventilation and positive end expiratory pressure results in survival of approximately 50 percent of patients. Only minimal abnormalities in lung function are found in long-term survivors.

THE ADULT RESPIRATORY DISTRESS SYNDROME (ARDS) is best defined as clinical-pathophysiological state characterized by severe dyspnea, hypoxemia and diffuse bilateral pulmonary infiltrations following acute lung injury in previously healthy persons, usually with no prior major lung disease. This review describes the clinical presentation, discusses the current state of our knowledge of pathogenesis and presents an approach to systematic, physiologically oriented management. Prognosis and late sequellae of ARDS are also reviewed.

Historical Perspective

ARDS is not new to medicine. Our original characterization of ARDS[1,2] cited earlier descriptions of the pathologic conditions related to ARDS, previously termed congestive atelectasis.[3] Today ARDS is recognized as an important clinical state and is better understood and better managed, although substantial problems with management remain. Rapidly growing interest in ARDS has resulted in an increasing number of editorial comments, some using other names for the syndrome,[4-6] and some controversy over the appropriateness of the use of ARDS as a proper designation of the clinical syndrome has surfaced.[7,8]

From the Division of Pulmonary Sciences and the Webb-Waring Lung Institute, University of Colorado Medical Center, Denver.

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Reprint requests to: Thomas L. Petty, MD, Professor of Medicine, Head, Division of Pulmonary Sciences, Box C 273, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver, CO 80262.

Two multidisciplinary conferences concerning ARDS served to indicate that ARDS occurred following a variety of unrelated lung injuries[9,10] and that many loosely used clinical terms, listed in Table 1, actually refer to the same entity (ARDS).

ARDS was first described as a clinical syndrome[1] in 1967. In 12 patients clinical features were reported that were believed "remarkably similar to the infantile respiratory distress syndrome." Ventilatory management with positive end expiratory pressure (PEEP) was also first reported in ARDS in that article, although the technique of PEEP had been described earlier.[11] Five patients survived. Autopsy findings in the seven who died showed striking alveolar atelectasis, engorgement of capillaries and hyaline membrane formation.[1]

Shortly after this, in February 1968, a conference on the pulmonary effects of nonthoracic trauma was conducted in Washington, D.C., by the Committee on Trauma of the Division of Medical Sciences, National Academy of Sciences—National Research Council.[9] Discussion of the pulmonary effects of shock accompanying multiple long bone trauma and following resuscitation often involving large volumes of fluid showed that the pulmonary features had a monotonous regularity and a striking similarity to those in our original description of ARDS.[9] Many of the presentors were clinicians who had cared for combat casualties in Vietnam. It was believed that a large number of cases coming to the attention of physicians was due to huge numbers of

TABLE 1.—*Other Terms for Adult Respiratory Distress Syndrome*

Shock lung
Traumatic wet lung
White lung syndrome
Capillary leak syndrome
Acute alveolar failure
Post-perfusion lung
DaNang lung
Congestive atelectasis
Adult hyaline membrane disease

combat casualties cared for by "alert informed physicians whose minds have been sensitized to detect the unusual and the unexplained."[9] The excellent battlefield resuscitation and prompt evacuation to surgical care facilities made it possible for persons who previously would have died to receive medical attention.

The mechanisms of acute lung injury *were and remain unknown,* but speculations regarding toxic factors or vasoactive substances, the pulmonary effects of fat embolization, lung ischemia, surfactant abnormalities, hemodynamic factors and exogenous factors such as overtransfusion of fluids were considered as possibly involved in the pathogenesis of ARDS.

One of us (T.L.P.) reported 21 cases at this conference. A new therapeutic approach was described which included mechanical ventilation with a newly designed volume respirator, PEEP, fluid restriction and corticosteroid drugs. In this series, 11 of 14 patients survived with the use of PEEP compared with only 3 of 8 during our earliest experience where PEEP was not used. There was, therefore, a suggestion of improved survival with PEEP in this early series ($p = <0.05$).[12]

Later a clearer clinical description of ARDS was offered, stressing clinical features, factors influencing prognosis and principles of management,[2] and the 16th Aspen Lung Conference on acute pulmonary injury and repair dealt with basic science and clinical aspects of ARDS.[10] Subsequently there have been many excellent studies originating from other centers that have added greatly to our understanding of ARDS.

Clinical Setting and Clinical Presentation

The clinical onset of ARDS may be dramatic or insidious. Often there is a latent period between the initial injury (such as shock or multiple trauma) and the subsequent full development of the clinical, roentgenographic and pathophysiological features.

TABLE 2.—*Adult Respiratory Distress Syndrome*

A. *Clinical Signs*
Pronounced dyspnea
Tachypnea
Labored respirations
Intercostal retractions
Cyanosis, refractory to oxygen therapy
B. *X-ray and Physiologic Signs*
Diffuse bilateral pulmonary infiltrates
Reduced lung and chest wall compliance $\Delta V/\Delta P$ (measured on ventilator)
Increased alveolar or inspired to arterial oxygen tension difference
Improved pulmonary oxygen transport with positive end expiratory pressure
High minute ventilation (spontaneous or with a ventilator)

Since ARDS occurs following a variety of direct and indirect lung insults the clinical presentation as well as the manifestations of the clinical syndrome itself will be a consequence of the type of injury. These findings are summarized briefly in Table 2. Respiratory distress, labored respirations, diffuse monotonous bilateral infiltrates and profound hypoxemia are hallmarks of the syndrome. The respiratory rate and minute ventilation are high.[13]

Interestingly, the physical examination is not often very revealing. The labored respirations are obvious, and cyanosis, known to be an unreliable sign of hypoxemia, may or may not be present. On auscultation of the lungs very few abnormal sounds are heard in spite of the pronounced respiratory distress and massive pulmonary infiltrations of the fully developed syndrome. Specifically the bubbling rales of cardiogenic pulmonary edema, the rhonchi of secretions in large airways and the crackling rales of pulmonary fibrosis are not heard. One generally hears a harsh short inspiratory phase and a rather normal expiratory phase during mechanical ventilation. Cardiac sounds are usually normal with no third or fourth heart sound and no valvular murmurs unless there is associated myocardial trauma.

Pathophysiology

Laboratory determinations measured at the bedside with the patient receiving mechanical ventilation help show the pathophysiology in a clinically useful way. Overall pulmonary compliance, the sum of lung and chest wall compliances, is notably decreased. This can be easily measured in patients receiving mechanical ventilation by dividing the delivery pressure of the

ventilator into the tidal volume delivered by the machine. Maintaining static pressure on the lungs and thorax by holding the lungs at end inspiration by occluding the exhalation manifold, or by using the inflation hold control available on some respirators, allows a static compliance measurement to be made. In our original series of 12 patients the overall effective compliance ranged from 9 to 19 ml per cm of water compared with normal values in our laboratory of 75 to 125 ml per cm. This is evidence of the notably impaired overall compliance due to "stiff lungs." High minute ventilation (which is many times more than 20 liters per minute) is present and can be measured with a simple hand spirometer (Wright, for example) or calculated from ventilator rate and tidal volume. Profound hypoxemia is usually present in spite of high inspired oxygen fractions, with accompanying hypocarbia due to the high minute ventilation.

The difference between inspired and arterial oxygen tensions is indicative of the difficulty with oxygen transfer across the lung and is probably a more useful bedside test than the measurement of alveolar to arterial tension difference during ventilation with 100 percent oxygen, as is commonly done in some intensive respiratory care units. We prefer this method of assessing the impairment in oxygen transfer across the lungs because it deals with the arterial tension at which the patient is receiving mechanical ventilation and avoids the artifact of increasing the alveolar arterial tension difference on 100 percent oxygen breathing which converts low ventilation perfusion regions into shunt regions.[2] The underlying physiological basis for the gas transfer abnormality is severe ventilation-perfusion ($\dot{V}_A\dot{Q}$)[14] mismatch and wasted ventilation which affects arterial oxygenation a great deal more than carbon dioxide elimination. A true diffusion defect may be present as well due to interstitial edema, hyaline membrane formation and a reduced capillary blood volume.[15,16]

The basis of the mechanical derangement of ARDS lungs is not clearly known. Increased elastic and surface forces are present and are considered in the discussion of surfactant below.

Roentgenograms of the Chest

The features seen on x-ray studies of the chest are monotonously similar despite the many different pathways to the development of ARDS. Generally diffuse, bilateral dense alveolar infiltrates are present without pleural effusions or enlargement of the cardiac silhouette, unless there is a related myocardial injury or pericardial effusion as a consequence of the original lung injury (Figure 1). It must be stressed that the x-ray features are not specific for the nature or degree of acute pulmonary insult and do not accurately correlate with the degree of physiologic abnormality present. Occasionally infiltrations are somewhat unilateral, often in the presence of direct lung trauma with contusion (Figure 2).

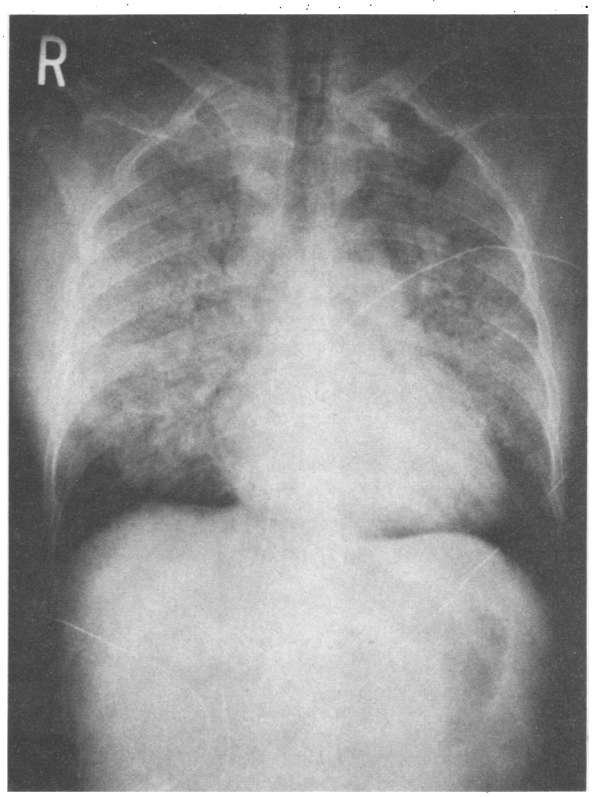

Figure 1.—Typical x-ray appearance of ARDS in 46-year-old woman following severe hemorrhagic shock. Note bilateral alveolar infiltrates with air bronchograms.

Theories of Pathogenesis

It is apparent that the lung can be injured by insults delivered via the airways or circulation.[17] Causes leading to these remarkably similar clinical features include shock from any cause (hemorrhagic, cardiogenic, septic or even anaphylactoid),[18] multiple trauma including massive fat embolization,[19] diffuse intravascular coagulation,[20] endotoxin,[21] paraquat poisoning,[22] drowning,[23] overwhelming viral pneumonias,[24] massive aspiration[25] and central nervous system injury[26] including trauma and drugs (especially narcotic drugs).[27,28] Therefore, many possibilities concern-

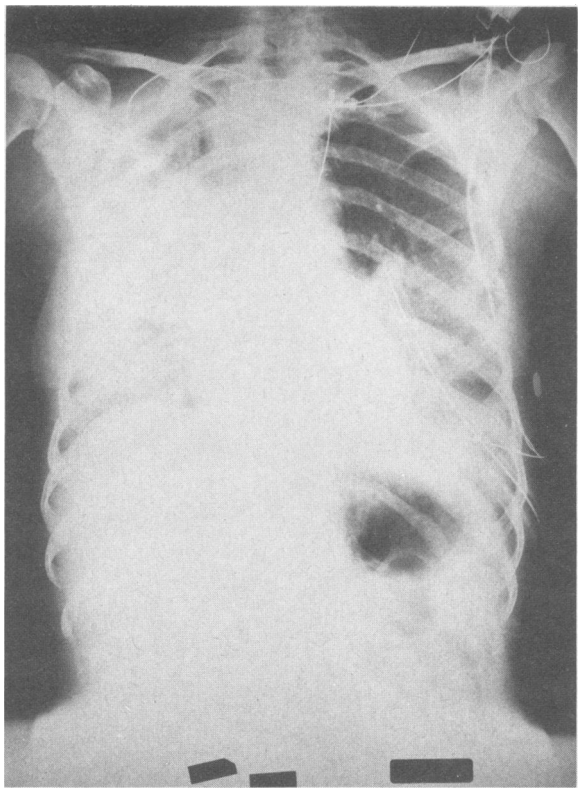

Figure 2.—X-ray appearance of lung contusion in ARDS following automobile trauma in 34-year-old woman. Severe contusion of right lung is present.

ing the exact mechanism of injury exist. Possible agents or mechanisms involved in diffuse lung injury are cited in Table 3.

From the above a "final common pathway" must occur following these diverse insults which injure the lung *either* via the inhaled route or via the circulation. There is strong evidence to support the hypothesis of increased capillary permeability leading to "capillary leak."[25,30,31]

Pathological Findings

The lungs are heavy, airless and appear like liver in cut sections. Alveoli are collapsed, and a hemorrhagic infiltration with debris and hyaline membranes are found lining alveolar spaces. These pathologic features are nonspecific and represent the final common pathway of massive diffuse lung injury.[1,9]

Experimental Models

Several experimental models have been used to produce a clinical-pathological syndrome in some ways similar to ARDS. The most widely used is the injection of oleic acid into large animals, mostly dogs.[32] A chest trauma model producing pulmonary contusion[33] and a hemorrhagic shock model also caused features similar to those in ARDS in dogs[34,35] and in primates.[36]

TABLE 3.—*Possible Causes of Adult Respiratory Distress Syndrome*

Leukocytes
Platelets
Humoral agents
Immunological reactions
Neurogenic shock
Oxygen
Microemboli
Toxins
Overhydration
Viral infections
Complement

Various disturbances of brain function, including anemia and shock, lead to abnormalities in brain oxidative phosphorylation. These are believed operative in ARDS and form the basis for "neurogenic models."[26,36] The likelihood of a neurogenic mechanism is supported by evidence that denervation of one lung offers protection against damage, with severe lung edema occurring in the contralateral innervated lung.[36,37]

High oxygen concentrations have been used to create a pattern of lung injury in lambs similar to that found in ARDS; this same injury did not occur in lambs receiving ventilation in a similar manner with air.[38] This model supports the belief that oxygen-induced injury is a major factor in further lung injury during the treatment of ARDS in humans[39,40] (see discussion of oxygen and ventilation below).

Leukocytic sequestration occurring in experimental hypotension with release of proteolytic enzymes,[41] the effect of platelet aggregates[42] with release of humoral agents and the mechanical effects of cellular microemboli are believed to play a role in lung injury at least in experimental models and possibly in ARDS.[43,44] An aspiration injury model using hydrochloric acid with a pH of 1.8 on a dose weight basis in dogs offers an additional experimental approach.[45]

Although the scientific advantages of an experimental model are obvious, species differences in lung structure and differences in response to various types of injury make comparisons of these models difficult. Their relevance to ARDS, consequently, is subject to question.

Role of Surfactant Abnormalities

The increased elastic recoil of ARDS, the shared features with the respiratory distress syndrome of the newborn[46] and the suggestion of surfactant

abnormalities in some,[34] but not all[35] of the above cited experimental models have focused attention on possible surfactant abnormalities in ARDS. A primary surfactant abnormality cannot, of course, be implicated, but the possibility of surfactant inactivation in states of pulmonary edema has been raised.[47] Secondary surfactant abnormalities could then contribute to the pathogenesis of ARDS.[48] The hypothesis is that alveolar atelectasis would augment the transudation of pulmonary edema and hemorrhage, thereby leading to massive focal atelectasis. The fact that a latent period of often 12 to 24 hours or more occurs between acute lung injury and the development of ARDS is intriguing in this regard since it is known that surfactant half-life (on release from the type II pneumocyte) is approximately 18 to 24 hours after experimental pulmonary embolization and recovery.[49]

Considerable evidence exists that type II cells and probably surfactant production can be damaged by high oxygen concentrations, which are often required for life support in severe states of ARDS.[50,51]

Although our original report suggested surfactant abnormalities from observations made on minced lung specimens,[1] it was not until recently that we were able to show abnormalities in surfactant compressibility and in the isopycnic density of the alveolar lipoprotein aggregates in a fresh specimen from a patient with ARDS following severe hemorrhagic shock.[52] Shortly thereafter we found similar abnormalities in surfactant function in five additional ARDS cases due to septicemia and narcotic overdose with aspiration alone and hemorrhagic shock, respectively.[53]

Therefore, although the role of surfactant abnormalities remains speculative the existence of surfactant abnormalities is now strongly suggested. The role of surfactant in the further pathogenesis of ARDS following the initial injury and its role in the mechanical improvement which can be observed clinically (see below) on recovery parallels the necessary time for recovery and regeneration of type II cells. Both the experimental and clinical observations, therefore, have credibility in relation to the pathogenesis of ARDS.

Incidence

The true incidence of ARDS in the United States today is not known. This is due largely to lack of uniformity and agreement on definition, and no effective reporting mechanism. The task force of the lung division of the National Heart, Lung and Blood Institute has estimated that at least 150,000 cases are identified and treated each year.[44] The true incidence is probably much greater.

Management

Prevention

Ideally ARDS should be anticipated and prevented. This means the avoidance of fluid overload whenever possible, the utilization of the lowest possible oxygen fraction for adequate tissue oxygenation and, at least in the case of multiple long bone fractures, the institution of corticosteroid drugs to prevent or anticipate the adverse effects of free fatty acids on the lung in the dramatic syndrome of fat embolization.[19] There are other considerations for steroids discussed below.

Supportive Management

Many reviews describing the current state of the art have been offered.[2,30,48,54,55] In brief, the treatment of the full-blown syndrome is primarily supportive and requires the placement of a definitive airway and mechanical ventilation using a ventilator with high pressure and flow capability. An endotracheal tube can be placed initially and is suitable for short-term management, such as two to four days. Endotracheal tubes can be left in place longer but they have the disadvantages of poor patient comfort, are an inferior route for suctioning and do not usually allow the patient to take nourishment by mouth.

A volume ventilator providing high pressure and flow capability and accurate control of the inspired oxygen fraction is required. The ventilator provides mechanical work and allows modification of pressure wave forms. The Monaghan 225 and 228 respirators and the Bennett MA-1 respirator, along with others, offer the necessary pressure and flow capabilities required in most cases of ARDS. To avoid possible oxygen toxicity, it is important to reduce the inspired oxygen fraction as rapidly as possible while maintaining adequate oxygen transport across the lungs commensurate with tissue demands. The possibilty of further oxygen induced injury must be minimized with the use of the lowest possible oxygen fraction. Most modern ventilators have accurate control of oxygen fraction delivery. These have been summarized in various textbooks. The time-

dose threshold in producing oxygen toxicity in man remains unknown. An extensive review considers this subject.[56,57]

Positive end expiratory pressure also improves oxygen transport across the lung by reducing shunting.[1,2,13,57,61] Very likely, lung units are recruited with the use of PEEP. Functional residual capacity is clearly increased.[60,61] Since pressures on the order of 5 to 15 cm water are generally all that is required, it is unlikely that cardiac output will be significantly reduced.[62] Some investigators employ much higher levels of PEEP.[63]

In some circumstances tissue oxygen transport may, in fact, be reduced by PEEP[38,64] and the possibility of barotrauma may be increased in high levels of PEEP. Therefore, a concept of optimal PEEP is emerging.[65,66] Optimum PEEP as judged by systemic oxygen transport, usually occurs within the best compliance region ($\Delta V/\Delta P$) of mechanical ventilation.[65,66]

Initially the mechanical ventilator is adjusted with a fairly high tidal volume of 12 to 14 ml per kg and the machine used in the assister-controller mode. The routine measurement of pressure-volume curves of lungs and thorax is recommended in order to establish the tidal volume and PEEP level which exist within the region of best overall compliance.[65,67]

It is preferable whenever possible not to paralyze patients. Even with crush injuries of the chest many patients will allow the ventilator to provide the work of breathing in the combined assister-controller mode with a rate chosen appropriate for the patients' needs. The application of the modern ventilator of course must be guided by frequent arterial blood gas determinations.

Fluid Management

Proper fluid management is essential in maintaining an adequate circulation and avoiding further complications. Whereas aggressive fluid therapy was the rule in shock management before the characterization of ARDS,[68] it subsequently became clear that fluid overload is an important complicating factor in ARDS.[1,2,13,55] Fluid sequestration in the lung is probably facilitated by increased capillary permeability. In addition, fluid retention as a response to ventilator management via excessive antidiuretic hormone activity is a likely complicating factor.[69] Nonetheless adequate systemic perfusion is mandatory in order to maintain organ system integrity including the lung.[70]

The choice of fluid replacement remains controversial. Albumin replacement to restore the delicate Starling relationship between hydrostatic and colloid pressure has been suggested in patients with ARDS and interstitial edema who are hypoproteinemic.[71] Other experimental evidence indicates, in contrast, that lung water may actually be increased with the use of colloid compared with crystalloid infusions.[72] For this reason and on the basis of bedside clinical experience, the authors today prefer the use of crystalloid solutions. Diuretics such as furosemide or ethacrynic acid are also employed if there is overt evidence of fluid overload and systemic circulation is satisfactory. In the most difficult cases one often walks the proverbial tightrope—balancing between fluid administration, monitoring evidence of adequate perfusion such as systemic blood pressure, adequate urine flow (such as 25 to 30 ml per hour), and the avoidance of overhydration using the pulmonary capillary wedge pressure measured through a Swan-Ganz catheter as a guide.[73] Renal function may become a relatively low priority during this period and mild to moderate azotemia is common. Even advancing renal failure should not demand a pronounced increase of fluid infusion.

Adjunctive Pharmacologic Management

Certain groups of drugs are commonly used during the ventilatory support phase of ARDS care. A brief commentary on corticosteroids, antibiotics and fluid management follows.

Corticosteroids have a theoretic benefit by their ability to prevent or reduce aggregation of leukocytes which may cause damage by the release of proteolytic enzymes within the lung. Some authors have offered the view that corticosteroids are protective in the face of endotoxic shock by reducing the activity of lysosomal enzymes.[74,75] Methylprednisolone has increased the survival rate in dogs with lung injury induced by oleic acid.[76] It has also been suggested from observations in humans and in experimental animal models that corticosteroids are effective in fat embolization.[19,77] Also, improved mechanics was found in excised rat lungs following exposure to high oxygen concentrations, with improved survival with corticosteroids compared with controls.[78]

Against the use of steroids is their potential effect of reducing lung bacterial clearance, shown

in experimental studies.[79] We have reported that sepsis complicating ARDS remains an unsolved enigma.[80]

Whether or not steroids have other therapeutic benefits or disadvantages is not known. In practice, the authors use methylprednisolone sodium succinate (30 mg per kg of body weight, given intravenously in divided dosage) for the first 24 to 48 hours. In theory this will capitalize upon the beneficial effects and minimize long-term side effects such as sepsis and oxygen toxicity.

Antibiotics

The use of prophylactic antibiotics is to be condemned. In a review of our earlier experience there was no evidence that the use of prophylactic antibiotics in any way prevented infection with dangerous Gram-negative bacilli.[80] Therefore, use of antibiotics should be reserved for identified infections and then guided by culture and sensitivity tests.

Strategies of Care

The priorities are (1) adequate arterial oxygenation (for example, arterial oxygen saturation [SaO_2], 90 percent) and adequate circulating hemoglobin to maintain oxygen content; (2) adequate cardiac output (for example, sufficient for mixed venous oxygen pressure [Po_2] greater than 30 mm of mercury) and (if possible to observe) adequate mentation or integrated central nervous system responses, warm extremities and some renal flow, (3) lowest possible fraction of inspiratory oxygen (FIO_2), ideally to 0.6 or less within 24 hours and to 0.5 or less after two or three days. Naturally there are trade-offs in these strategies and, of course, the *bottom line* is adequate oxygenation and maintenance of brain function.

Weaning

Mechanical ventilatory support is required until the patient recovers sufficiently to support his or her own ventilation, and to adequately transfer oxygen without PEEP. Briefly, the chest must be stable, the patient alert and cooperative and PEEP no longer required. PEEP should not be reduced until the inspired oxygen concentration can be reduced to 40 percent (FIO_2 less than 0.4) and then PEEP should be reduced in 3 cm of water increments with repeated monitoring of blood gases both initially and one hour after each reduction. At this stage, if oxygen transport is adequate, short trials with a T-piece attached to the endotracheal tube or tracheostomy collar are made with blood gas monitoring at 30 to 60 minute intervals. If blood gases are maintained and the patient remains comfortable, the ventilatory assistance is no longer needed and the endotracheal tube or tracheostomy can be removed, if not needed as an independent airway. Further details of useful weaning techniques in ARDS are cited elsewhere.[81]

Prognosis

The immediate outcome in ARDS involves three basic factors: (1) the degree of original lung injury, (2) the success of initial resuscitation and support of the patient and (3) the avoidance of complications and further injury. Certainly there are patients whose lung injury is so severe that survival is not possible. These patients often die shortly after they reach the hospital. Properly applied support methods will generally permit the immediate survival of most patients in spite of severe lung injury. Modern mechanical ventilators provide sufficient work capability to support the ventilation of even severely damaged lungs. In most patients adequate oxygenation can be accomplished at the onset with high inspired oxygen fractions (tensions); however, this is at the cost of potential further lung injury from oxygen toxicity. It must be emphasized that it is extremely important to minimize the likelihood of oxygen toxicity by carrying out mechanical ventilation with the lowest possible inspired oxygen fraction (see principles of management). Avoidance of septic complications is equally important.

Observations can be made at the bedside which are good prognostic indicators. Patients with the best compliance and the best and most prompt blood gas response to PEEP are most likely to recover.[82] Open lung biopsy studies in those with more unfavorable physiologic measures showed the greatest cellular and fibrotic changes.[82]

The comparison of survival rates from various institutions is difficult because of different selection criteria. Our own experience in 100 consecutive patients managed at our center, beginning with our first case, from 1966 to 1975, is cited in Table 4. It is evident that the overall survival is not improving, but it must be stressed that eight patients in whom liver transplantation was done, all of whom died with sepsis, are included in the

last 50 cases. Without these special cases the survival rate in our overall series is 49 percent which is similar to that in other series.[44]

Sequellae on Recovery

Late sequellae are surprisingly infrequent. In a series of ten patients with ARDS requiring mechanical ventilation for from 3 to 36 days (mean 13.5 days) from an FIO_2 greater than 0.6 for 2 to 13 days (mean 4.6 days), four were entirely asymptomatic and six had only mild to moderate symptoms when carefully evaluated 4 to 42 months after recovery (mean 23 months).[81] The physiological abnormalities were only mild to moderate and included both obstructive and restrictive ventilatory abnormalities, a moderate diffusion defect which tended to improve with time, and normal blood gas values at rest, but slight hypoxemia during exercise. Others have reported similar findings.[82,83] A reevaluation in nine of our original patients (follow-up 39 to 83 months after ARDS) showed a further improvement in patients with a restrictive ventilatory defect and stable minimal airflow obstruction or normal lung function except in one person with underlying chronic obstructive pulmonary disease.[84] Interestingly, airway hyperreactivity with increased response to methacholine was found in two of 7 patients tested.

The morphologic basis for lung recovery from severe diffuse injury is suggested by the work of Bachofen and Weibel[16] who have shown that the type I alveolar lining cell is geometrically too complex to replicate and, therefore, if injured, dies. Type II or so-called metabolically active cells, however, can proliferate and differentiate into type I cells to reestablish the alveolar capillary membrane.[16] That this occurs is highly suggested by the gradual improvement shown in forced vital capacity, functional residual capacity, single breath diffusion tests and arterial blood gas studies on recovery.[83-86]

The Future

We need to understand mechanisms of disease and how the lung responds to injury and how repair may occur without fibrosis. We desperately need markers of injury by which we can detect ARDS *before* the advanced syndrome is recognized clinically. We must find ways to induce oxygen tolerance and protect the lung from sepsis. We must learn the role of surfactant abnormalities in the pathogenesis of the syndrome. So far, new approaches to support using an extracorporeal oxygenator for partial oxygenation of severely injured patients have not proved more successful than conventional means of support. A few long-term survivors have been reported, however.[87,88] It is possible that this form of support would be more successful if applied to less severe cases. The key to success is to protect the lung from further injury during the life-support period and the challenge is to reduce the risk of sepsis and oxygen toxicity.

TABLE 4.—*Survival in Adult Respiratory Distress Syndrome*

Year	*1967*[1]	*1972*[80]	*1975*
Patients	12	51	100
Survived	5	21	45
Percent	42	41	45

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